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EDITORIAL COMMENT

Echocardiographic Understanding of Secondary Mitral Regurgitation in Transcatheter Mitral Valve Repair

More to Learn*

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Transcatheter mitral valve repair (TMVr) with MitraClip (Abbott Structural Heart, Santa Clara, California) is now approved by the U.S. Food and Drug Administration in patients with symptomatic moderate-severe to severe secondary mitral regurgitation (SMR) who failed maximally tolerated guideline-directed medical therapy (GDMT). This was based on the positive results of the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial that showed MitraClip plus GDMT was superior to GDMT alone in certain heart failure patients with SMR (1). However, the 2-year outcomes of the MITRA-FR (Percutaneous Repair with the Mitral Device for Severe Functional Secondary Mitral Regurgitation) trial showed no benefit in TMVr versus GDMT (2). One of the key differences between the 2 trials were the echocardiographic severity of MR and extent of left ventricular (LV) dysfunction in the enrolled population. Given the variability in the echocardiographic assessment of SMR, Asch et al. (3) in this issue of the *Journal,* described the echocardiographic qualification process in COAPT and evaluated parameters that affected outcomes (3). Based on their pre-defined echocardiographic criteria, the authors found that the benefit of TMVr encompassed all echocardiographic subgroups, independent of LV dysfunction and dilatation, pulmonary hypertension, severity of tricuspid regurgitation, or MR characteristics.

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There are 3 takeaways from this important study. First, we all know that MR is dynamic and quantitative evaluation can be challenging due to technical factors and potential measurement errors. To attempt to overcome these limitations, the COAPT core laboratory established a multiparametric algorithm to determine echocardiographic characteristics in the enrollees and found that 85.7% of patients are in tier 1 (i.e., effective regurgitant orifice area [EROA] $\geq$0.3 cm^2 or pulmonary vein systolic flow reversal). However, the remaining patients enrolled in the trial had EROA $<$0.3 cm^2 but had other echocardiographic features deemed to qualify for the trial, including regurgitant volume $\geq$45 ml/beat, regurgitation fraction $\geq$40%, vena contracta width $\geq$0.5 cm, proximal isovelocity surface area radius $>$0.9 cm, and large jet wrapped around the left atrium. However, regurgitant volume and regurgitation fraction assessments were feasible in only 42.3% of patients, and paired-analysis was only available in 11.4% of patients. Despite this, the authors found that patients across all 3 tiers of echocardiographic evaluation benefited from TMVr in COAPT. Given the limitations in assessing MR quantitatively, we must therefore be more proactive in using this multiparametric approach to quantify MR severity to determine which SMR patients we see in our practice will match the COAPT echocardiographic criteria and benefit from

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mitral intervention. Unfortunately, this is rarely done.

Second, that the severity of LV dysfunction and dimensions were not predictors of 2-year outcomes in the TMVr group was surprising. The same authors previously showed that patients with EROA <0.30 cm^2 and left ventricular end-diastolic volume index >96 ml/m^2 (n = 56, 10.2% of enrollees, MITRA-FR–like patients) and ≤ 96 ml/m^2 (n = 51, 9.3%) had no difference in 1-year all-cause mortality and heart failure hospitalization between groups (4). This discrepancy may be due to the 2-year data not yet available in this subgroup at the time of initial data reporting, but may also suggest a more complex interaction between the dysfunctional left ventricle and mitral apparatus leading to SMR. In fact, we know that SMR is a heterogeneous entity, caused by asymmetric or symmetric tethering. Some SMR, using this multiparametric evaluation, may benefit from TMVr despite advanced LV dysfunction or dilatation. The challenge is to identify the subgroup of patients who will not benefit from mitral intervention. What we do know is that patients with LVEF <20% and LVESD >70 mm were outside of the COAPT inclusion criteria, and therefore it cannot be determined whether TMVr will benefit in these patients. This is important to keep in mind when we consider this paper's findings in our daily practice. Interestingly, we have not yet seen any data on patients who died or were hospitalized in either the MitraClip or GDMT group. Understanding these subgroups is perhaps more educational so we can better learn to screen out the "Cohort C" type patients in SMR.

Last, it appears that TMVr had no effect in promoting reverse LV remodeling in the COAPT population, even though it attenuates the progressive increase in LV dimensions and decline in LV function. This finding was disappointing, but it makes sense given that edge-to-edge repair was not designed to target the underlying mechanism of SMR, namely ventricular disease. It would be interesting to see if LV remodeling devices may have additive benefits to TMVr in these patients. Nonetheless, the evidence thus far clearly shows that in certain patients with symptomatic and echocardiographically important SMR, the clinical benefit of TMVr persists at least to 3 years, including patients on GDMT alone who crossed over at 2 years to mitral intervention (5).

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